Docket No.: HO-P02703US2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Atul Varadhachary	Real Party in Interest: Agennix Inc.
Application No.: 10/728,521	Confirmation No.: 8270
Filed: December 5, 2003	Art Unit: 1656
For: ORAL LACTOFERRIN IN THE TREATMENT OF SEPSIS	Examiner: C. M. Kam

REPLY BRIEF

STATUS OF CLAIMS

The Application filed on December 5, 2003 contained claims 1-44. Prior to examination, claims 1-20 and 26-40 were elected pursuant to a restriction requirement mailed October 20, 2004. Following an Office Action mailed January 10, 2005, a response was filed on April 11, 2005 canceling claims 2-6, 11-13, 21-25, 33-37, and 41-44; adding claims 45-46; and amending claims 1, 26, 27, 31, 32, and 38. Following an Office Action mailed June 17, 2006, a response was filed on September 19, 2005 amending claims 1, 8-10, 15, 16, 26-28, 31, 32, and 38; and canceling claims 45-46. Following an Office Action mailed December 5, 2005, a response was filed on February 13, 2006 amending claims 1, 8-10, 15, 16, 26, 27, 31, 32, and 38. Following an Office Action mailed April 24, 2006, a response was filed on September 26, 2006 amending claims 1, 26, 27, 31, 32, and 38. Following an Office Action mailed December 6, 2006, a response was filed in which no amendments to the claims were made.

A Final Office Action was mailed on July 5, 2007 rejecting the pending claims 1, 7-10, 14-20, 26-32 and 38-40. Applicant filed a Notice of Appeal on October 2, 2007 and corresponding Appeal brief was filed on April 2, 2008. The Examiner Answer was mailed June 10, 2008.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1, 7, 14, 17-20, 26-32 and 38-40 were rejected under 35 U.S.C. § 103(a) as being obvious over Van Bree *et al.* (WO 01/72322, Exhibit A, "Van Bree").

Claims 1, 7-10, 14-20, 26-32 and 38-40 were rejected under the judicially created doctrine of obviousness type double patenting.

ARGUMENT

The Examiner's Answer to the Appellant's Appeal Brief does not fully consider the Appellant's arguments. In particular the Answer does not address the primary point of contention regarding oral administration of lactoferrin for bacteremia. This reply brief sets out to further clarify the Appellant's position and distinctly point out the fallacies of the Examiner's position.

Van Bree does not teach oral dosages to treat bacteremia or sepsis

The main point of contention is on whether Van Bree makes obvious the use of oral administration of lactoferrin in an effective amount to treat bacteremia or sepsis as recited in the instant claims. Appellants assert that this is not the case.

The Appellants point to the "Field of the Invention" section of Van Bree which specifically states that their invention "relates to the production, purification and use of recombinant human lactoferrin for parenteral administration in various therapeutic applications." (emphasis added) Addressing the limitation of oral dosage to treat bacteremia or sepsis, the Appellants note that the MPEP distinctly lays out the legal concept of *Prima Facie* obviousness in section 2142. A relevant passage is quoted below:

> To reach a proper determination under 35 U.S.C. 103, the examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of applicant's disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences," conduct the search and **evaluate the "subject matter as a whole" of the invention**. The tendency to resort to "hindsight" based upon applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.

(emphasis added). The determination under 35 U.S.C. 103(a) must be reached by resolving if a person of ordinary skill in the art would consider the instant invention obvious given the prior art disclosure (Van Bree), and common knowledge in the art at the time, such as that included in Exhibit B ("Kuhara").

The relevant disclosures of Van Bree are listed herein. Van Bree teaches use of lactoferrin by parenteral administration (page 3, lines 3-4) to treat diseases and conditions that require a bolus of and/or sustained large doses (page 3, lines 15-16). Van Bree teaches that high dosage parenteral administration of lactoferrin or lactoferrin variants (page 18, lines 1-2) has indications such as treating microbial infections (page 19, line 3), anti-inflammatory, anti-viral and anti-infective activities (page 19, lines 24-4), pro- and anti-coagulant effects (page 19, lines 3-4), anti-tumor effects (page 19, line 26), treatment of rheumatoid arthritis and ulcerative colitis (page 22, line 20), and treatment of iron storage diseases (page 23, lines 6-7). Specifically Van Bree teaches intraperitoneal injection of lactoferrin inhibits growth of solid tumors (page 22, lines 32-33), and high dose intravenous administration of human lactoferrin as an anti-coagulant to counteract the effects of heparin (page 34, lines 12-16). Van Bree also discloses oral treatment for infections or disorders of the digestive tract (page 26, lines 22-24). Van Bree catalogues multiple general forms of administration including food additives, nutritional supplements, parenteral (preferably intravenous), intradermal, topical, enteral, intramuscular and oral (in conjunction with parenteral) (page 23, lines 21-26). Finally, Van Bree teaches that "**[t]he particular form of the composition varies with the intended mode of administration and therapeutic application.**" (Van Bree, page 27, lines 9-10) This speaks directly towards Van Bree's disclosure of the treatment of bacterimia and sepsis with high doses of lactoferrin by parenteral routes, while disclosing that treatment of gastric infections and disorders of the digestive tract with oral administration of lactoferrin.

It was known to one of skill in the relevant art at the time that lactoferrin is not systemically bioavailable when ingested, and that high oral doses of lactoferrin do not significantly raise plasma lactoferrin levels (Kuhara, page 197, lines 8-10). Given this knowledge, one of skill in the art would not assume that parenteral administration and oral administration were equivalent. Further, as stated above, Van Bree discloses that the form of the composition varies with the intended mode of administration and therapeutic application (Van Bree, lines 9-10). Thus, it was not obvious to substitute parenteral routes with oral routes, since the therapeutically needed high levels of lactoferrin achieved by parenteral administration (e.g. intravenous) would not be reached in the blood by an oral treatment. Effectively, Kuhara teaches away from using oral dosages of lactoferrin to treat the

conditions and diseases that Van Bree discloses as needing high dosage parenteral administration, such as bacteremia and sepsis.

Further, oral dosages are disclosed by Van Bree *only in conjunction with corresponding parenteral administration*. "Oral administration can also be used, optionally but not necessarily, in conjunction with parenteral administration." (emphasis added) The only point in Van Bree where oral treatment is mentioned outside of a corresponding parenteral treatment is when discussing oral treatment for infections of, or disorders of the digestive tract (page 26, lines 22-24). One of skill in the art would know that one intended mode of administration to treat digestive tract issues would be oral treatment. However, the instant claims recite the treatment of bacteremia and sepsis, which Van Bree teaches to be treated by the intended parenteral route of administration.

One of skill in the art would have read the disclosures of Van Bree in context. However, the Examiner has cited elements from the prior art without regard to the context surrounding each disclosure. The Examiner's flawed argument is that Van Bree discloses treatment of bacteremia with high dose intravenous lactoferrin, optionally with oral lactoferrin supplementation, and Van Bree discloses oral formulations of lactoferrin; thus, one of skill in the art would find it obvious that an oral dose of lactoferrin could be provided in an effective amount for bacteremia. By this same logic, Van Bree discloses treatment of infant anemia with iron loaded lactoferrin in baby formula (page 23, lines 3-18), and Van Bree discloses topical lactoferrin formulations (page 23, lines 22-24); thus, one of skill in the art would find it obvious to treat infant anemia with an effective amount of a topically applied lactoferrin formulation. The Appellants assert that neither case is obvious given the disclosures of Van Bree, even in view of the fact that, *e.g.*, topical lactoferrin compositions and lactoferrin for infant anemia are disclosed on the same page. Obviousness is not established by virtue of textual proximity alone, nor does such proximity free the Examiner from having to provide the required articulated reasoning for the conclusion of obviousness.

The Examiner has not issued a 102 rejection, because Van Bree does not interrelate the elements disclosed therein in a way that meets the pending claims. The Examiner instead goes to great lengths to attempt to create the appearance of obviousness by citing individual passages from Van Bree, without regard for the context of each passage. The Supreme Court

has held that demonstrating that the claimed elements exist in the prior art is insufficient to find obviousness, rather, reasons for prompting a person of skill in the art to combine the elements as claimed must be identified. *KSR v. Teleflex,* 550 U.S. ___, 82 U.S.P.Q.2d 1385, 1396 (2007), (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). This refusal of the Examiner to acknowledge the context of the cited passages has blinded her to what one of skill in the art would have deemed obvious given the disclosures of the prior art. One of skill in the art would not have combined the elements as claimed because there was no reason one of skill in the art would have done so. Further, there existed art at the time that would have taught away from such a modification. The Examiner's ultimate conclusion is thus an impermissible, hindsight driven reconstruction, which only makes sense by resorting to the Applicant's own disclosure.

CONCLUSION

Appellants have provided arguments that overcome the pending rejection. Elements not addressed in this Reply Brief have been fully addressed in the Appeal Brief and are left out of the Reply Brief for efficiency. Appellants respectfully submit that the Answer's conclusions that the rejection of the claims should be sustained are unwarranted. It is therefore requested that the Board overturn the rejection of the Action.

Applicant believes no fee is due with this Reply Brief. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02703US2 from which the undersigned is authorized to draw.

Dated: July 23, 2008

Respectfully submitted,

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